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- N Engl J Med. 1999 Jan 28;340(4):318-9.

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The sentinel node in breast cancer--a multicenter validation study.

Krag D, Weaver D, Ashikaga T, Moffat F, Klimberg VS, Shriver C, Feldman S, Kusminsky R, Gadd M, Kuhn J, Harlow S, Beitsch P.

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BACKGROUND: Pilot studies indicate that probe-guided resection of radioactive sentinel nodes (the first nodes that receive drainage from tumors) can identify regional metastases in patients with breast cancer. To confirm this finding, we conducted a multicenter study of the method as used by 11 surgeons in a variety of practice settings. METHODS: We enrolled 443 patients with breast cancer. The technique involved the injection of 4 ml of technetium-99m sulfur colloid (1 mCi [37 MBq]) into the breast around the tumor or biopsy cavity. "Hot spots" representing underlying sentinel nodes were identified with a gamma probe. Sentinel nodes subjacent to hot spots were removed. All patients underwent a complete axillary lymphadenectomy. RESULTS: The overall rate of identification of hot spots was 93 percent (in 413 of 443 patients). The pathological status of the sentinel nodes was compared with that of the remaining axillary nodes. The accuracy of the sentinel nodes with respect to the positive or negative status of the axillary nodes was 97 percent (392 of 405); the specificity of the method was 100 percent, the positive predictive value was 100 percent, the negative predictive value was 96 percent (291 of 304), and the sensitivity was 89 percent (101 of 114). The sentinel nodes were outside the axilla in 8 percent of cases and outside of level 1 nodes in 11 percent of cases. Three percent of positive sentinel nodes were in nonaxillary locations. CONCLUSIONS: Biopsy of sentinel nodes can predict the presence or absence of axillary-node metastases in patients with breast cancer. However, the procedure can be technically challenging, and the success rate varies according to the surgeon and the characteristics of the patient.

Publication Types:
- Multicenter Study

PMID: 9753708 [PubMed - indexed for MEDLINE]

1: J Natl Cancer Inst 1978 Oct;61(4):967-78 Related Articles, Links

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Isolation of two human tumor epithelial cell lines from solid breast carcinomas.

Lasfargues EY, Coutinho WG, Redfield ES.

Most of the available human breast tumor cell lines have been derived from pleural effusions. The two cell lines herein described, BT-474 and BT-483, were derived from solid, invasive ductal breast carcinomas. Both are epithelial and neoplastic as judged by their general morphology, their fine structure, and their ability to produce growing nodules in nude mice and colonies in soft agar and methocel. BT-474 and BT-483 are human as expressed by chromosome morphology and aneuploid with a modal number of 55 and 72 chromosomes, respectively. Trypsin-Giemsa banding did not reveal the presence of obvious HeLa markers, and the glucose 6-phosphate dehydrogenase electrophoretic migration pattern was of the B-type. Furthermore, the migration of lactic dehydrogenase, malic dehydrogenase, and 6-phosphogluconate dehydrogenase isoenzymes was consistent with a human pattern and different from that of the mouse, rat, or hamster. Quarterly tests to detect the presence of aerobic and anaerobic mycoplasmas were repeatedly negative. A culture medium containing insulin, increased amounts of amino acids, vitamins, and glucose facilitated the isolation of the tumor cells. Cell replication was maintained with 10% fetal calf serum absorbed with activated charcoal and dextran. No production of alpha-lactalbumin was detected by radioimmunoassays, but high levels of progesterone receptors were found in both cell lines.

PMID: 212572 [PubMed - indexed for MEDLINE]

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Radioimmunoscintigraphy in patients with breast adenocarcinoma using technetium-99m labelled monoclonal antibody 170H.82: report of a phase II study.

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McQuarrie SA, MacLean GD, Boniface GR, Golberg K, McEwan AJ.

University of Alberta, Edmonton, Alberta, Canada.

Fifty-three women with clinical evidence of adenocarcinoma of the breast were studied with technetium-99m labelled monoclonal antibody (MAb) 170H.82 at protein doses of 1, 2 and 4 mg. An overall per lesion efficacy of 83.5% sensitivity and 97.7% positive predictive value was obtained. Efficacy appears higher in lesions restricted to the breast and local regional disease than systemic metastases. For the 2 mg dose the breast/local regional disease efficacy was 90% sensitivity and 90.2% positive predictive value. The biodistribution of this MAb was best represented by a two-compartment model with a distribution-phase half-life of 4.0+/-1.4 h, followed by an elimination-phase half-life of 39.6+/-6.6 h. In all six patients studied, the critical organ was the kidney, with a mean radiation absorbed dose of 37+/-6.9 mGy/GBq. The accuracy of this imaging technique allows the development of diagnostic strategies for the routine use of the compound in patients with breast cancer.

Related Resources

Publication Types:
- Clinical Trial
- Clinical Trial, Phase II
- Randomized Controlled Trial

PMID: 9096088 [PubMed - indexed for MEDLINE]

1: Cancer Biother Radiopharm 1997 Oct;12(5):305-16 Related Articles, Links

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A CDR-grafted (humanized) domain-deleted antitumor antibody.

Slavin-Chiorini DC, Kashmiri SV, Lee HS, Milenic DE, Poole DJ, Bernon E, Schlom J, Hand PH.

Laboratory of Tumor Immunology and Biology, National Cancer Institute, National Institutes of Health Bethesda, Maryland 20892, USA.

While several murine monoclonal antibodies (MAbs) directed against carcinoma associated antigens have shown excellent tumor targeting properties in clinical trials, the use of radiolabeled MAbs for both diagnostic and therapeutic applications has been hindered by two factors: (a) the induction of host anti-immunoglobulin (Ig) responses and (b) slow plasma clearance of unbound radiolabeled MAb, resulting in bone marrow toxicity for therapeutic application, and long intervals between MAb administration and tumor detection for diagnostic applications. This report describes the development of the first recombinant Ig with properties designed to reduce or eliminate both of the above problems: a complementarity determining region (CDR)-grafted humanized (Hu) MAb with a CH2 domain deletion (delta CH2). The MAb chosen for engineering was CC49, which is directed against a pancarcinoma antigen designated TAG-72 that is expressed on the majority of colorectal, gastric, breast, ovarian, prostate, pancreatic and lung carcinomas. When characterized for antigen binding in solid phase competition radioimmunoassays, the HuCC49 delta CH2 MAb completely inhibited the binding of murine (mu) CC49 and HuCC49 for TAG-72. The relative affinity constants (Ka) of MAbs HuCC49 delta CH2, HuCC49 and muCC49 were 5.1 x 10(-9), 2.1 x 10(-9) and 2.3 x 10(-9), respectively. The plasma clearance of 131I-HuCC49 delta CH2 was significantly faster than that of intact 125I-HuCC49 after either i.v. or i.p. administration in athymic mice (p(2)0.05). Biodistribution studies in athymic mice bearing human colon carcinoma xenografts after i.v. or i.p. administration of 131I-HuCC49 delta CH2 and 125I-HuCC49 demonstrated the efficient tumor localization and substantially lower percent of the injected dose (%ID/g) of the HuCC49 delta CH2 in normal tissues. This is reflected in the significantly higher radiolocalization indices (%ID/g in tumor divided by %ID/g in normal tissue) observed with the HuCC49 delta CH2 for most normal tissues tested (p(2)0.05). The differential between the rate of plasma clearance of HuCC49 delta CH2 and HuCC49 was even more

pronounced in SCID mice, which have been shown to be an appropriate model to study the metabolism of human IgG. These studies thus describe the development of a recombinant Ig molecule which, for the first time, combines 1) the properties of more rapid blood clearance than an intact humanized Ig molecule--without loss of antigen binding affinity--and 2) reduced potential for eliciting a human anti-murine antibody (HAMA) response in patients. These studies also demonstrate the potential utility of HuCC49 delta CH2 for i.p. as well as i.v. radioimmunodiagnosis and radioimmunotherapy in patients with TAG-72 positive tumors.

PMID: 10851481 [PubMed - indexed for MEDLINE]
